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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/715,066	11/17/2003	Timothy O'Brien	022438.45514	6392

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EXAMINER	
REDDIG, PETER J	

ART UNIT	PAPER NUMBER
1642	

MAIL DATE	DELIVERY MODE
08/08/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/715,066	O'BRIEN ET AL.	
	Examiner	Art Unit	
	PETER J. REDDIG	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 May 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2,21,22 and 27-29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2,21,22 and 27-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/8/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The Amendment filed May 8, 2008 in response to the Office Action of January 10, 2008 is acknowledged and has been entered. Previously pending claim 1 has been cancelled; claims 2, 21, 22, 27, and 28 have been amended and new claim 29 have been added.

2. Claims 2, 21, 22, 27, 28 and 29 are currently being examined.

3. Applicant's request for reconsideration of the finality of the rejection of the last Office action is persuasive and, therefore, the finality of that action is withdrawn as set forth in the summary of the interview of 05 May 2008.

New Grounds of Rejection

Priority

4. Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 119(e) as follows:

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The disclosure of the prior-filed applications fails to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for claims 21, 22, 27, and 28 of this application. Examiner has established a priority date of 11/17/2003 for claims 21,

22, 27, and 28 because the claims as currently constituted recite isolated nucleic molecules that are adapted to express or encode specific residues of SEQ ID NO: 5 and a review of the parent Applications does not reveal the claimed limitations, see the written description rejection in section 6 below. Additionally, the priority date of claims 2 and 29 is November 15, 2002, based on application 60/427,045 being the prior filed application in which a nucleic acid comprising SEQ ID NO: 4 is present, i.e. SEQ ID NO: 314 of application 60/427,045. Applicant is invited to submit evidence pointing to the serial number, page and line where support can be found establishing an earlier priority date.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 2, 21, 22, 27, 28 and 29 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 27, and its dependent claim 2, are indefinite in that claim 27 is drawn to an isolated nucleic acid molecule encoding residues 10,432 to 22,152 of SEQ ID NO:5 or a fragment of residues 10,432 to 22,152 of SEQ ID NO:5; wherein the isolated nucleic acid molecule is an expression vector and is adapted to express in a cell residues 10,432 to 22,152 of SEQ ID NO:5 or a fragment of residues 10,432 to 22,152 of SEQ ID NO:5;wherein the fragment of residues 10,432 to 22,152 of SEQ ID NO:5 is an antigenic fragment that can be used to make monoclonal antibodies that specifically recognize CA125 and cannot be determined if the claim is limited to isolated nucleotides only encoding and expressing the fragment of residues 10,432 to 22,152 of

SEQ ID NO:5 or a fragment thereof, or if the claims encompass nucleic acids that encode and express fragments larger than residues 10,432 to 22,152 of SEQ ID NO:5.

It will be assumed for examination purposes that the claim is drawn to an isolated nucleic acid molecule encoding *a polypeptide comprising* residues 10,432 to 22,152 of SEQ ID NO:5 or *a polypeptide comprising* a fragment of residues 10,432 to 22,152 of SEQ ID NO:5; wherein the isolated nucleic acid molecule is an expression vector and is adapted to express in a cell residues *a polypeptide comprising* 10,432 to 22,152 of SEQ ID NO:5 or *a polypeptide comprising* a fragment of residues 10,432 to 22,152 of SEQ ID NO:5;wherein the fragment of residues 10,432 to 22,152 of SEQ ID NO:5 is an antigenic fragment that can be used to make monoclonal antibodies that specifically recognize CA125.

Claim 28, and its dependent claims, claims 21, 22, and 29, are indefinite in that claim 28 is drawn to an isolated nucleic acid molecule encoding CA125 (SEQ ID NO:5) or a fragment thereof wherein the isolated nucleic acid molecule is an expression vector and is adapted to express in a cell CA125 (SEQ ID NO:5) or a fragment thereof . . . wherein the isolated nucleic acid molecule encodes residues 1 to 10,431 of SEQ ID NO:5 or a fragment of residues 1 to 10,431 of SEQ ID NO:5, and it can not be determined if the isolated nucleic molecule is also adapted to express residues 1 to 10,431 of SEQ ID NO: 5 or a fragment of residues 1 to 10,431 of SEQ ID NO:5 or if it is only required to encode them and not necessarily express them. In other words, it is unclear if the claim is limited to a polynucleotide adapted to express residues 1 to 10,431 of SEQ ID NO: 5 or a fragment of residues 1 to 10,431 of SEQ ID NO:5 or if polynucleotides expressing fragments larger than residues 1 to 10,431 of SEQ ID NO:5 are encompassed by the claim.

It will be assumed for examination purposes that the isolated nucleic acid molecules are in an expression vector and are adapted to express in a cell SEQ ID NO: 5 or a fragment thereof that comprise a nucleic acid molecule that encodes residues 1 to 10,431 of SEQ ID NO:5 or a fragment of residues 1 to 10,431 of SEQ ID NO:5, wherein the fragment thereof is an antigenic fragment that can be used to make monoclonal antibodies that specifically recognize CA125 (SEQ ID NO: 5). Thus, the claims are interpreted as being drawn to polynucleotides encoding and expressing a protein that comprises at least a fragment of residues 1 to 10,431 of SEQ ID NO:5.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 21, 22, 27, 28 and 29 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In regard to claim 27, the limitation of an isolated nucleic acid molecule encoding residues 10,432 to 22,152 of SEQ ID NO:5 or a fragment of residues 10,432 to 22,152 of SEQ ID NO:5; wherein the isolated nucleic acid molecule is an expression vector and is adapted to express in a cell residues 10,432 to 22,152 of SEQ ID NO:5 or a fragment of residues 10,432 to 22,152 of SEQ ID NO:5;wherein the fragment of residues 10,432 to 22,152 of SEQ ID NO:5 is

an antigenic fragment that can be used to make monoclonal antibodies that specifically recognize CA125 has no clear support in the specification and the claims as originally filed.

Applicants argue that claim 27 is supported, e.g., by SEQ ID NO: 162 of parent provisional application serial no. 60/427,045, which is identical to residues 10,432-22,152 of SEQ ID NO: 5.

The suggested support is not found persuasive because, although SEQ ID NO: 162 may be identical to residues 10,432-22,152 of SEQ ID NO:5, this polypeptide does not provide support for the genus of claimed nucleic acids encoding or adapted to express the specifically claimed residues of SEQ ID NO: 5 or fragments thereof.

Applicants argue that claim 27 is also supported, e.g., by SEQ ID NOS:34, 36, and 38 in Tables 14, 16, and 18 of parent provisional patent application serial no. 60/299,380, which are disclosed to be the amino terminal domain, repeat domain, and carboxy terminal domain of CA125 and together make residues 10,432-22,152 of SEQ ID NO:5.

The suggested support is not found persuasive because, although SEQ ID NOS:34, 36, and 38 may make residues 10,432-22,152 of SEQ ID NO:5, these individual polypeptides do not provide support for the genus of claimed nucleic acids encoding or adapted to express the specifically claimed residues of SEQ ID NO: 5 or fragments thereof.

Applicants argue that claim 27 is also supported, e.g., by originally filed claims 1, 4, 14, and 15. Originally filed claims 14 and 15 disclose fragments of SEQ ID NO:5 and antibodies that bind to SEQ ID NO:5 and fragments thereof.

The suggested support is not found persuasive. Originally filed claims 1, 4, 14, and 15 are drawn to: 1. An isolated nucleic acid molecule encoding CA125. 4. The isolated nucleic acid

molecule of claim 2 wherein said molecule is a fragment thereof. 14. A polypeptide with the amino acid sequence selected from the group consisting of: (a) the amino acid sequence set forth in SEQ ID NO: 5; (b) an amino acid sequence having at least 50% sequence identity to said sequence; (c) a conservative variant of an one of (a) to (b); and (d) a fragment of any one of (a) to (c). 15. A purified antibody that selectively binds to an amino acid sequence of the CA125 protein: (a) wherein the amino acid sequence of the CA125 protein comprises the amino acid sequence set forth in SEQ ID NO: 5; (b) an amino acid sequence having at least 50% sequence identity to said sequence; (c) a conservative variant of any one of (a) to (b); and (d) a fragment of any one of (a) to (c). Originally filed claims 1, 4, 14, and 15 do provide support for or suggest the genus of claimed nucleic acids encoding or adapted to express the specifically claimed residues of SEQ ID NO: 5 or fragments thereof.

Applicants argue that claim 27 is also supported by provisional patent application serial no. 60/299,380 as follows. Pages 19-20 of provisional patent application serial no. 60/299,380 discloses recombinant domains and epitopes of CA125 and antibodies against recombinant domains. Pages 6-7 of provisional patent application serial no. 60/299,380 disclose isolated nucleic acids and fragments of the nucleic acids isolated, and expressing isolated nucleic acids from vectors. Page 2, first line of the Summary of provisional patent application serial no. 60/299,380 discloses isolating portions of the CA 125 gene. Page 3, lines 5-10 and page 4, line 3 of provisional patent application serial no. 60/299,380 disclose use of recombinant domains, such as individual repeat units, of CA 125. Page 3, lines 15-18 of provisional patent application serial no. 60/299,380 disclose recombinant domains of CA125 encompassing epitope binding

sites for murine antibodies. There is thus abundant support for isolated nucleic acids used to express fragments of CA125 that can be used to generate antibodies that recognize CA125.

The suggested support is not found persuasive because the cited passages of application serial no. 60/299,380 do not provide support for or suggest the claimed nucleic acid encoding or adapted to express the specifically claimed residues of SEQ ID NO: 5 or fragments thereof. Given the above the subject matter claimed in claim 27 broadens the scope of the invention as originally disclosed in the specification.

In regard to claim 28 and its dependent claims 21, and 22, the limitation of the isolated nucleic acid molecule is an expression vector and is adapted to express in a cell CA125 (SEQ ID NO:5) or a fragment thereof . . . wherein the isolated nucleic acid molecule encodes residues 1 to 10,431 of SEQ ID NO:5 or a fragment of residues 1 to 10,431 of SEQ ID NO:5 has no clear support in the specification and the claims as originally filed.

Applicants argue that claim 28 is supported, e.g., by SEQ ID NO: 310 of parent provisional patent application serial no. 60/427,045, which is identical to residues 1-10,431 of SEQ Id NO:5.

The suggested support is not found persuasive because, although SEQ ID NO: 310 may be identical to residues 1-10,431 of SEQ ID NO:5, this polypeptide does not provide support for the genus of claimed nucleic acids encoding or adapted to express the specifically claimed residues of SEQ ID NO: 5 or fragments thereof.

Applicants argue that claim 28 is also supported, e.g., by originally filed claims 1, 4, 14, and 15, by SEQ ID NO:5, and by paragraphs [0009], [0011], and [0041] of the specification, and by SEQ ID NOS: 1 and 4. Paragraph [0009] discloses that the extracellular amino terminal

domain is encoded by exons 1-9, as set out in SEQ ID NO: 1. It discloses that exon 4 is nucleotides 34575 to 38024 of SEQ ID NO:I. Paragraphs [0011] and [0041] disclose that the amino terminal extension comprises (is encoded by) four genomic exons [exons 1-4 described in paragraph 0009]. A comparison of the sequence of exon 4 (nucleotides 34575-38024 ofSEQ ID NO:l) and the cDNA of SEQ ID NO:4 reveals that exon 4 ends at nucleotide 31,485 of SEQ ID NO:4. A comparison of the sequences of exons 1-4 of SEQ ID NO: 1, the cDNA sequence of SEQ ID NO: 4, and the protein sequence of SEQ ID NO:5 reveals that exons 1-4 encode residues 1-10,427 of SEQ ID NO:5. Applicants argue that Claim 21 is supported, e.g., by SEQ ID NO: 1 and paragraph [0009]. Applicants argue that the element of fragments of SEQ ID NO:5 recognized by an antibody that selectively binds to SEQ ID NO:5 is supported, e.g., by originally filed claim 15, part (d), and claim 14.

The suggested support is not found persuasive. Originally filed claims 1, 4, 14, and 15 are drawn to: 1. An isolated nucleic acid molecule encoding CA125. 4. The isolated nucleic acid molecule of claim 2 wherein said molecule is a fragment thereof. 14. A polypeptide with the amino acid sequence selected from the group consisting of: (a) the amino acid sequence set forth in SEQ ID NO: 5; (b) an amino acid sequence having at least 50% sequence identity to said sequence; (c) a conservative variant of an one of (a) to (b); and (d) a fragment of any one of (a) to (c). 15. A purified antibody that selectively binds to an amino acid sequence of the CA125 protein: (a) wherein the amino acid sequence of the CA125 protein comprises the amino acid sequence set forth in SEQ ID NO: 5; (b) an amino acid sequence having at least 50% sequence identity to said sequence; (c) a conservative variant of any one of (a) to (b); and (d) a fragment of any one of (a) to (c). Originally filed claims 1, 4, 14, and 15 do provide support for or suggest the

claimed nucleic acid encoding or adapted to express the specifically claimed residues of SEQ ID NO: 5 or fragments thereof. Additionally the polypeptide of SEQ ID NO: 5 does not support or suggest the genus of claimed nucleic acids encoding or adapted to express the specifically claimed residues of SEQ ID NO: 5 or fragments thereof. Additionally, the disclosure of the individual exons of CA125 and SEQ ID NO: 4, although exons 1-4 may encode residues 1-10,427 of SEQ ID NO:5, does not support or suggest the genus of claimed nucleic acids encoding or adapted to express the specifically claimed residues of SEQ ID NO: 5 or fragments thereof

Additionally, although an isolated nucleic acid molecule comprising the sequence of SEQ ID NO: 1 in an expression vector would inherently express at least a fragment of residues 1-10,431 of SEQ ID NO:5, there is not inherent support for fragments of SEQ ID NO: 1 encoding and expressing residues 1-10,431 of SEQ ID NO:5 or fragments thereof.

Given the above the subject matter claimed in claims 21, 22 and 28 broadens the scope of the invention as originally disclosed in the specification.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claim 27 is rejected under 35 U.S.C. 102(b) as being anticipated by Yin and Lloyd (J. Biol. Chem. July 20, 2001. 276: 27371-27375, previously cited) and evidenced by appendix 1.

Yin and Lloyd teach cloning a C-terminal fragment of CA125 by screening a λZAP cDNA expression library of cDNA from OVCAR3 cells with an antibody to CA125, see Abstract, Materials and Methods, p. 27,372, and the Figures. Given that the λZAP cDNA vectors express fragments of cDNA that are detected by a CA125, Lin and Lloyd teach an isolated expression vector with a fragment of SEQ ID NO: 4 encoding a fragment of CA125 that is adapted to express in a cell a fragment of SEQ ID NO: 5 that is a fragment of residues 10,432 to 22,152 of SEQ ID NO: 5, see appendix 1.

Given that the polynucleotide of the prior art reference encodes a polypeptide that is recognized by an antibody to CA125, it would be expected that the encoded fragment could be used to make monoclonal antibodies that specifically recognize CA125. Although the reference does not specifically state that the isolated CA125 nucleotide fragment can be used to make monoclonal antibodies that specifically recognize CA125, the claimed product appears to be the same as the prior art product, absent a showing of unobvious differences. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA).

Applicants argue that claim 27 has a priority date of at least June 19, 2001. Claim 27 is fully supported by provisional patent application 60/299,380, which was filed June 19, 2001. SEQ ID NOS:34, 36, and 38 in Tables 14, 16, and 18 of parent provisional patent application serial no. 60/299,380 are disclosed to be the amino terminal domain, repeat domain, and carboxy

terminal domain of CA125. Together these make up residues 10,432-22,152 of SEQ ID NO: 5 as is recited in claim 27. Pages 6-7 of provisional patent application serial no. 60/299,380 disclose isolated nucleic acids and fragments of the nucleic acids isolated, and expressing isolated nucleic acids from vectors. Page 2, first line of the Summary of provisional patent application serial no. 60/299,380 discloses isolating portions of the CA125 gene. Page 3, lines 5-10 and page 4, line 3 of provisional patent application serial no. 60/299,380 discloses use of recombinant domains, such as individual repeat units, of CA125. Page 3, lines 11-18 of provisional patent application serial no. 60/299,380 discloses recombinant domains of CA 125 encompassing epitope binding sites for murine antibodies, and use of the recombinant molecules as vaccines or to stimulate patients' immune systems. There is thus abundant support for expressing fragments of CA 125 that can be used to generate antibodies that recognize CA125, as is recited in claim 27. The priority date of claim 27 is thus before Yin and Lloyd, and Yin and Lloyd is not prior art to claim 27.

Applicants arguments have been considered, but have not been found persuasive because, although SEQ ID NOS:34, 36, and 38 may make residues 10,432-22,152 of SEQ ID NO:5, these individual polypeptides do not provide support for the genus of claimed nucleic acids encoding or adapted to express the specifically claimed residues of SEQ ID NO: 5 or fragments thereof. Additionally, the cited passages of application serial no. 60/299,380 do not provide support for or suggest the claimed nucleic acid encoding or adapted to express the specifically claimed residues of SEQ ID NO: 5 or fragments thereof. Thus the priority date of claim 27 is 11/17/2003 as set forth above.

Applicants argue that Yin and Lloyd (3. Biol. Chem., July 20, 2001, 276:27371-27375) states that the authors isolated a 5797-base pair sequence containing a stop codon but no clear 5' initiation sequence (abstract). And it is dated July 20, 2001. The alignment the Examiner shows, however, is with Genbank locus AF361486, which is 21,112 bp (not 5797 bp) and states that it was updated on Sept. 8, 2003.

Applicant submits with this response in an Information Disclosure Statement the revision history of AF361486 and AF361486 version 1 GI:14971109. The revision history shows that version GI: 14971109 is the earliest version of AF361486 and was submitted on July 20, 2001. In the version submitted on July 20, 2001, AF361486 only had 5797 nucleotides, the same as Yin and Lloyd. The next revision of AF361486 was on Aug. 26, 2003. Version GI: 14971109 encodes an 1890-amino-acid protein that is homologous to the carboxy terminal 1890 amino acid residues of the present SEQ ID NO:5 and appears to be the protein sequence disclosed in Yin and Lloyd. The 21,112 bp sequence of the present AF361486 was only submitted on September 8, 2003.

Applicants arguments have been considered, but have not been found persuasive because the date of publication of the Yin and Lloyed article and AF361486 is July 20, 2001, the priority date of claim 27 is 11/17/2003 as set forth above, and the sequence encodes and is adapted to express a fragment in a cell a fragment of SEQ ID NO: 5 that is a fragment of residues 10,432 to 22,152 of SEQ ID NO: 5.

8. Claim 27 is rejected under 35 U.S.C. 102(b) as being anticipated by O'Brien et al. (Tumor Biology 2001 Nov-Dec; 22(6):348-366, IDS item) as evidenced by O'Brien et al. (Tumor Biology 2002 May-Jun; 23(3):154-169, IDS item).

O'Brien et al. (2001) teach cloning a CA125 repeat domain into an expressing vector and expressing it in cells, see para. bridging page 349-350, and Fig. 4 and 5. O'Brien et al. (2002) teach that the repeat domains are with residues 10,432-22,152 of CA125, see Fig. 7.

Although the reference does not specifically state that the isolated CA125 nucleotide fragment can be used to make monoclonal antibodies that specifically recognize CA125, the claimed product appears to be the same as the prior art product, absent a showing of unobvious differences. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA).

9. Claims 21, 22, 27, and 28 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 2002/68579 (Venter et al. 6 September 2002) as evidenced by Appendix 2.

Venter et al. teach isolated nucleic acids encoding fragments of residues 1-10,427 and 10-432 to 22, 152, see Appendix 2.

Venter et al. teach placing the isolated nucleic acids of the invention into vectors, see p. 18, lines 4-15. Venter et al. teach vectors with promoters that modulate the expression of an operably linked sequence, see page 32, lines 1-26. Venter et al. teach producing proteins with the isolated nucleic acids of the invention, see p. 10 lines 18-30 and page 34, lines 1-8. One of skill in the art would immediately recognize vectors with promoters that modulate the expression of

an operably linked sequence as an expression vector to be used for the expression and production of proteins from the isolated sequences.

Although the reference does not specifically state that the isolated CA125 nucleotide fragment can be used to make monoclonal antibodies that specifically recognize CA125/SEQ ID NO: 5, the claimed product appears to be the same as the prior art product, absent a showing of unobvious differences. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA).

10. Claim 27 is rejected under 35 U.S.C. 102(b) as being anticipated by WO 2001/51513 (Algate et al. 19 July 2001) as evidenced by Appendix 3.

Algate et al. teach isolated nucleic acids encoding fragments of residues 10,432 to 22, 152, see Appendix 3. Algate et al. teach putting the nucleic acids of the invention into expression vectors encoding the polypeptides in host cells, see page 2, lines 11-15.

Although the reference does not specifically state that the isolated CA125 nucleotide fragment can be used to make monoclonal antibodies that specifically recognize CA125, the claimed product appears to be the same as the prior art product, absent a showing of unobvious differences. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the

contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA).

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

11. Claims 2, 21, 22, 27, 28, and 29 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 48-50 and 52-55 of copending Application No. 11/975,668 in view of in view of US Patent No. 4,889,806 and Sambrook et al (Molecular Cloning, A Laboratory Manual, Cold Spring Harbor, 1989, p. 16.3-36).

Claims 48-50 and 52-55 of Application No. 11/975, 668 are drawn to are drawn to a an isolated nucleic acid encoding a polypeptide comprising a fragment of CA125 (SEQ ID NO:315)

selected from the group consisting of: (i) residues 1-1637 of SEQ ID NO:299 and an antigenic fragment of residues 1-1637 of SEQ ID NO:299; (ii) a repeat unit selected from repeat units 1-63 of Table 16; (iii) SEQ ID NOS: 164-191,195-208, 210-220, 222-225,227-247, 250-254, 256-276, and 278-293, ; and (iv) SEQ ID NO:300. The isolated nucleic acid of claim 50 wherein the nucleic acid encodes a polypeptide comprising SEQ ID NO:315. An isolated nucleic acid encoding a polypeptide comprising CA 125 (SEQ ID NO:315) or a fragment thereof; wherein the polypeptide comprises residues 1-10,427 of SEQ ID NO:310 or an antigenic fragment of residues 1-10,427 of SEQ ID NO:310.

It is noted that SEQ ID NO: 315 of 11/975,668 is the full length CA125 protein which is identical to the full length CA125/ SEQ ID NO: 5 of the instant application and SEQ ID NO: 314 11/975,668 is identical to SEQ ID NO: 4 of the instant application. Thus, SEQ ID NO: 4 is clearly contemplated as a polynucleotide encoding the CA125 protein.

US Patent No. 4,889,806 teach that with the advent of recombinant DNA and molecular cloning technology it is now conventional to transfer genetic information into plasmids or vectors constructed in vitro and then transferred into host cells to be clonally propagated (col 1, lines 18-24).

Sambrook et al teach that cloned genes are conventionally expressed using expression vectors and that expression of cloned proteins have been used to: (1) confirm the identity of a cloned gene by using immunological or functional assays to detect the encoded protein; (2) produce large amounts of proteins of biological interest that are normally available in only limited quantities from natural sources; (3) to study the biosynthesis and intracellular transport of proteins following their expression in various cell types; and (4) to elucidate structure-function

relationships by analyzing the properties of normal and mutant proteins (para bridging pages 16.3 and 16.4).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to put the CA125 nucleic acids of copending Application No. 11/975, 668 in expression vectors as taught by Sambrook et al and US Patent No. 4,889,806 because US Patent No. 4,889,806 specifically teaches that it is conventional to transfer genetic materials into plasmids or vectors and then transfer the plasmids or vectors into host cells and clonally propagate the genetic material and because Sambrook et al teach that cloned genes are conventionally expressed using expression vectors. One of ordinary skill in the art at the time the invention was made would have been motivated to put the sequences of U.S. Patent No. 6, 261,836 in plasmid vectors operably linked to promoters as Sambrook et al and US Patent No. 4,889,806 because Sambrook et al specifically teach that expressed cloned proteins are used to: (1) confirm the identity of a cloned gene by using immunological or functional assays to detect the encoded protein; (2) produce large amounts of proteins of biological interest that are normally available in only limited quantities from natural sources; (3) to study the biosynthesis and intracellular transport of proteins following their expression in various cell types; and (4) to elucidate structure-function relationships by analyzing the properties of normal and mutant proteins.

This is a provisional obviousness-type double patenting rejection.

12. All other objections and rejections recited in January 10, 2008 are withdrawn.

13. No claims allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Peter J. Reddig whose telephone number is (571) 272-9031. The examiner can normally be reached on M-F 8:30 a.m.-5:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Peter J Reddig/

Examiner, Art Unit 1642

/P. J. R./

/Karen A Canella/
Primary Examiner, Art Unit 1643

Appendix 1.

```
LOCUS       AF361486               5797 bp    mRNA    linear   PRI 20-JUL-2001
DEFINITION  Homo sapiens mucin 16 (MUC16) mRNA, partial cds.
ACCESSION   AF361486
VERSION     AF361486.1  GI:14971109
KEYWORDS    .
SOURCE      Homo sapiens (human)
  ORGANISM  Homo sapiens
            Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
            Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
REFERENCE   1  (bases 1 to 5797)
  AUTHORS   Yin,B.W. and Lloyd,K.O.
  TITLE     Molecular cloning of the ca125 ovarian cancer antigen.
            identification as a new mucin, muc16
  JOURNAL   J. Biol. Chem. 276 (29), 27371-27375 (2001)
   PUBMED   11369781
REFERENCE   2  (bases 1 to 5797)
  AUTHORS   Lloyd,K.O. and Yin,B.W.T.
  TITLE     Direct Submission
  JOURNAL   Submitted (15-MAR-2001) Sloan-Kettering Institute for Cancer
            Research, 1275 York Ave., New York, NY 10021, USA
COMMENT     [WARNING] On Aug 26, 2003 this sequence was replaced by
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ORIGIN

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tumor marker CA125) (CA-125)
Score = 3693 bits (9577), Expect = 0.0, Method: Compositional matrix adjust.
Identities = 1845/1890 (97%), Positives = 1846/1890 (97%), Gaps = 0/1890 (0%)

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Sbjct  20383  LFKSTSVGPLYSGCRLTLLRPEKHGAATGVDAICTLRLDPTGPGLDRERLYWELSQLTNS  20442

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              EDMHRPGSRKFNTTERVLQGLLMPLFKNTSVSSLYSGCRLTLLRPEKDGAATRVDAVCTH
Sbjct  20983  EDMHRPGSRKFNTTERVLQGLLMPLFKNTSVSSLYSGCRLTLLRPEKDGAATRVDAVCTH  21042

Query  781    RPDPKSPGLDRERLYWKLSQLTHGITELGPYTLDRHSLYVNGFTHQSSMTTTRTPDTSTM  840
              RPDPKSPGLDRERLYWKLSQLTHGITELGPYTLDRHSLYVNGFTHQSSMTTTRTPDTSTM
Sbjct  21043  RPDPKSPGLDRERLYWKLSQLTHGITELGPYTLDRHSLYVNGFTHQSSMTTTRTPDTSTM  21102

Query  841    HLATSRTPASLSGPTTASPLLVLFTINFTITNLRYEENMHHPGSRKFNTTERVLQGLLRP  900
              HLATSRTPASLSGPTTASPLLVLFTINFTITNLRYEENMHHPGSRKFNTTERVLQGLLRP
Sbjct  21103  HLATSRTPASLSGPTTASPLLVLFTINFTITNLRYEENMHHPGSRKFNTTERVLQGLLRP  21162
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Query  901    VFKNTSVGPLYSGGCRLTLLRPKKDGAATKVDAICTYRPDPKSPGLDREQLYWELSQLTHS  960
              VFKNTSVGPLYSGGCRLTLLRPKKDGAATKVDAICTYRPDPKSPGLDREQLYWELSQLTHS
Sbjct  21163  VFKNTSVGPLYSGGCRLTLLRPKKDGAATKVDAICTYRPDPKSPGLDREQLYWELSQLTHS  21222

Query  961    ITELGPYTLDRDSLYVNGFTQRSSVPTTSIPGTPTVDLGTSGTPVSKPGPSAASPLLVLF  1020
              ITELGPYTLDRDSLYVNGFTQRSSVPTTSIPGTPTVDLGTSGTPVSKPGPSAASPLLVLF
Sbjct  21223  ITELGPYTLDRDSLYVNGFTQRSSVPTTSIPGTPTVDLGTSGTPVSKPGPSAASPLLVLF  21282

Query  1021   TLNFTITNLRYEEHMQHPGSRKFNTTERVLQGLLRSLFKSTSVGPLYSGCRLTLLRPEKD  1080
              TLNFTITNLRYEEHMQHPGSRKFNTTERVLQGLLRSLFKSTSVGPLYSGCRLTLLRPEKD
Sbjct  21283  TLNFTITNLRYEEHMQHPGSRKFNTTERVLQGLLRSLFKSTSVGPLYSGCRLTLLRPEKD  21342

Query  1081   GTATGVDAICTHHPDPKSPRLDREQLYWELSQLTHNITELGPYALDNDSLFVNGFTHRSS  1140
              GTATGVDAICTHHPDPKSPRLDREQLYWELSQLTHNITELG YALDNDSLFVNGFTHRSS
Sbjct  21343  GTATGVDAICTHHPDPKSPRLDREQLYWELSQLTHNITELGHYALDNDSLFVNGFTHRSS  21402

Query  1141   VSTTSTPGTPTVYLGASKTPASIFGPSAASHLLILFTLNFTITNLRYEENMWPGSRKFNT  1200
              VSTTSTPGTPTVYLGASKTPASIFGPSAASHLLILFTLNFTITNLRYEENMWPGSRKFNT
Sbjct  21403  VSTTSTPGTPTVYLGASKTPASIFGPSAASHLLILFTLNFTITNLRYEENMWPGSRKFNT  21462

Query  1201   TERVLQGLLRPLFKNTSVGPLYSGCRLTLLRPEKDGEATGVDAICTHRPDPTGPGLDREQ  1260
              TERVLQGLLRPLFKNTSVGPLYSG RLTLLRPEKDGEATGVDAICTHRPDPTGPGLDREQ
Sbjct  21463  TERVLQGLLRPLFKNTSVGPLYSGSRLTLLRPEKDGEATGVDAICTHRPDPTGPGLDREQ  21522

Query  1261   LYLELSQLTHSITELGPYTLDRDSLYVNGFTHRSSVPTTSTGVVSEEPFTLNFTINNLRY  1320
              LYLELSQLTHSITELGPYTLDRDSLYVNGFTHRSSVPTTSTGVVSEEPFTLNFTINNLRY
Sbjct  21523  LYLELSQLTHSITELGPYTLDRDSLYVNGFTHRSSVPTTSTGVVSEEPFTLNFTINNLRY  21582

Query  1321   MADMGQPGSLKFNITDNVMQHLLSPLFQRSSLGARYTGCRVIALRSVKNGAETRVDLLCT  1380
              MADMGQPGSLKFNITDNVM+HLLSPLFQRSSLGARYTGCRVIALRSVKNGAETRVDLLCT
Sbjct  21583  MADMGQPGSLKFNITDNVMKHLLSPLFQRSSLGARYTGCRVIALRSVKNGAETRVDLLCT  21642

Query  1381   YLQPLSGPGLPIKQVFHELSQQTHGITRLGPYSLDKDSLYLNGYNEPGPDEPPTTPKPAT  1440
              YLQPLSGPGLPIKQVFHELSQQTHGITRLGPYSLDKDSLYLNGYNEPG DEPPTTPKPAT
Sbjct  21643  YLQPLSGPGLPIKQVFHELSQQTHGITRLGPYSLDKDSLYLNGYNEPGLDEPPTTPKPAT  21702

Query  1441   TFLPPLSEATTAMGYHLKTLTLNFTISNLQYSPDMGKGSATFNSTEGVLQHLLRPLFQKS  1500
              TFLPPLSEATTAMGYHLKTLTLNFTISNLQYSPDMGKGSATFNSTEGVLQHLLRPLFQKS
Sbjct  21703  TFLPPLSEATTAMGYHLKTLTLNFTISNLQYSPDMGKGSATFNSTEGVLQHLLRPLFQKS  21762

Query  1501   SMGPFYLGCQLISLRPEKDGAATGVDTTCTYHPDPVGPGLDIQQLYWELSQLTHGVTQLG  1560
              SMGPFYLGCQLISLRPEKDGAATGVDTTCTYHPDPVGPGLDIQQLYWELSQLTHGVTQLG
Sbjct  21763  SMGPFYLGCQLISLRPEKDGAATGVDTTCTYHPDPVGPGLDIQQLYWELSQLTHGVTQLG  21822

Query  1561   FYVLDRDSLFINGYAPQNLSIRGEYQINFHIVNWNLSNPDPTSSEYITLLRDIQDKVTTL  1620
              FYVLDRDSLFINGYAPQNLSIRGEYQINFHIVNWNLSNPDPTSSEYITLLRDIQDKVTTL
Sbjct  21823  FYVLDRDSLFINGYAPQNLSIRGEYQINFHIVNWNLSNPDPTSSEYITLLRDIQDKVTTL  21882

Query  1621   YKGSQLHDTFRFCLVTNLTMDSVLVTVKALFSSNLDPSLVEQVFLDKTLNASFHWLGSTY  1680
              YKGSQLHDTFRFCLVTNLTMDSVLVTVKALFSSNLDPSLVEQVFLDKTLNASFHWLGSTY
Sbjct  21883  YKGSQLHDTFRFCLVTNLTMDSVLVTVKALFSSNLDPSLVEQVFLDKTLNASFHWLGSTY  21942

Query  1681   QLVDIHVTEMESSVYQPTSSSSTQHFYPNFTITNLPYSQDKAQPGTTNYQRNKRNIEDAL  1740
              QLVDIHVTEMESSVYQPTSSSSTQHFY NFTITNLPYSQDKAQPGTTNYQRNKRNIEDAL
Sbjct  21943  QLVDIHVTEMESSVYQPTSSSSTQHFYLNFTITNLPYSQDKAQPGTTNYQRNKRNIEDAL  22002

Query  1741   NQLFRNSSIKSYFSDCQVSTFRSVPNRHHTGVDSLCNFSPLARRVDRVAIYEEFLRMTRN  1800
              NQLFRNSSIKSYFSDCQVSTFRSVPNRHHTGVDSLCNFSPLARRVDRVAIYEEFLRMTRN
Sbjct  22003  NQLFRNSSIKSYFSDCQVSTFRSVPNRHHTGVDSLCNFSPLARRVDRVAIYEEFLRMTRN  22062
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Query  1801   GTQLQNFTLDRSSVLVDGYSPNRNEPLTGNSDLPFWAVILIGLAGLLGLITCLICGVLVT  1860
              GTQLQNFTLDRSSVLVDGYSPNRNEPLTGNSDLPFWAVILIGLAGLLGLITCLICGVLVT
Sbjct  22063  GTQLQNFTLDRSSVLVDGYSPNRNEPLTGNSDLPFWAVILIGLAGLLGLITCLICGVLVT  22122

Query  1861   TRRRKKEGEYNVQQQCPGYYQSHLDLEDLQ  1890
              TRRRKKEGEYNVQQQCPGYYQSHLDLEDLQ
Sbjct  22123  TRRRKKEGEYNVQQQCPGYYQSHLDLEDLQ  22152
```

Appendix 2

A. Alignment of amino acids 1-1000 of SEQ ID NO: 5 to the sequences of Venter et al.

```
AFS98121
ID   AFS98121 standard; DNA; 7521 BP.
XX
AC   AFS98121;
XX
DT   20-SEP-2007  (first entry)
XX
DE   Human transcript sequence, SEQ ID 17520.
XX
KW   DNA detection; RNA detection; exon; ds.
XX
OS   Homo sapiens.
XX
PN   WO200268579-A2.
XX
PD   06-SEP-2002.
XX
PF   10-JAN-2002; 2002WO-US000284.
XX
PR   10-JAN-2001; 2001US-00756696.
XX
PA   (PEKE ) PE CORP NY.
XX
PI   Venter CJ,  Adams M,  Li PWD,  Myers EW;
XX
DR   WPI; 2002-682812/73.
XX
PT   New isolated nucleic acid detection reagent for detecting the presence of
PT   specified human exons.
XX
PS   Claim 4; SEQ ID NO 17520; 40pp; English.
XX
CC   The present invention relates to a novel isolated nucleic acid detection
CC   reagent for detecting the presence of specified human exons. The exon
CC   sequences cover every identified human transcript and exon comprising
CC   every gene/coding region of the human genome. The present sequence is one
CC   such exon sequence. The nucleic acid detection agent is used for
CC   detecting the presence of at least 100000, at least 2000, at least 50000
CC   or at least 10000 human exons. The sequences that span exon-exon
CC   junctions eliminate false signals caused by genomic contamination. This
CC   is because a detection element comprising two neighboring exons as one
CC   contiguous sequence will not hybridize to genomic DNA comprising
CC   intervening intronic DNA. These detection elements will only hybridize to
CC   expressed mRNA transcripts in which the exons are connected and the
CC   intronic sequence has been removed, therefore forming one contiguous
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CC   stretch of sequence corresponding to the sequence of the detection
CC   element that spans the exon-exon junction.
XX
SQ   Sequence 7521 BP; 2172 A; 2277 C; 1433 G; 1639 T; 0 U; 0 Other;

Alignment Scores:
Pred. No.:                2.6e-154        Length:         7521
Score:                    4899.00         Matches:        980
Percent Similarity:       100.0%          Conservative:   0
Best Local Similarity:    100.0%          Mismatches:     0
Query Match:              98.0%           Indels:         0
DB:                       7               Gaps:           0

US-10-715-066A-5_COPY_1_1000 (1-1000) x AFS98121 (1-7521)

Qy          21 SerArgSerThrLysAlaThrProGluMetAspSerGlyLeuThrGlyAlaThrLeuSer 40
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db           3 AGCAGGAGCACTAAAGCCACACCAGAAATGGATTCAGGACTGACAGGAGCCACCTTGTCA 62

Qy          41 ProLysThrSerThrGlyAlaIleValValThrGluHisThrLeuProPheThrSerPro 60
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          63 CCTAAGACATCTACAGGTGCAATCGTGGTGACAGAACATACTCTGCCCTTTACTTCCCCA 122

Qy          61 AspLysThrLeuAlaSerProThrSerSerValValGlyArgThrThrGlnSerLeuGly 80
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         123 GATAAGACCTTGGCCAGTCCTACATCTTCGGTTGTGGGAAGAACCACCCAGTCTTTGGGG 182

Qy          81 ValMetSerSerAlaLeuProGluSerThrSerArgGlyMetThrHisSerGluGlnArg 100
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         183 GTGATGTCCTCTGCTCTCCCTGAGTCAACCTCTAGAGGAATGACACACTCCGAGCAAAGA 242

Qy         101 ThrSerProSerLeuSerProGlnValAsnGlyThrProSerArgAsnTyrProAlaThr 120
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         243 ACCAGCCCATCGCTGAGTCCCCAGGTCAATGGAACTCCCTCTAGGAACTACCCTGCTACA 302

Qy         121 SerMetValSerGlyLeuSerSerProArgThrArgThrSerSerThrGluGlyAsnPhe 140
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         303 AGCATGGTTTCAGGATTGAGTTCCCCAAGGACCAGGACCAGTTCCACAGAAGGAAATTTT 362

Qy         141 ThrLysGluAlaSerThrTyrThrLeuThrValGluThrThrSerGlyProValThrGlu 160
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         363 ACCAAAGAAGCATCTACATACACACTCACTGTAGAGACCACAAGTGGCCCAGTCACTGAG 422

Qy         161 LysTyrThrValProThrGluThrSerThrThrGluGlyAspSerThrGluThrProTrp 180
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         423 AAGTACACAGTCCCCACTGAGACCTCAACAACTGAAGGTGACAGCACAGAGACCCCCTGG 482

Qy         181 AspThrArgTyrIleProValLysIleThrSerProMetLysThrPheAlaAspSerThr 200
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         483 GACACAAGATATATTCCTGTAAAAATCACATCTCCAATGAAAACATTTGCAGATTCAACT 542

Qy         201 AlaSerLysGluAsnAlaProValSerMetThrProAlaGluThrThrValThrAspSer 220
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         543 GCATCCAAGGAAAATGCCCCAGTGTCTATGACTCCAGCTGAGACCACAGTTACTGACTCA 602

Qy         221 HisThrProGlyArgThrAsnProSerPheGlyThrLeuTyrSerSerPheLeuAspLeu 240
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         603 CATACTCCAGGAAGGACAAACCCATCATTTGGGACACTTTATTCTTCCTTCCTTGACCTA 662

Qy         241 SerProLysGlyThrProAsnSerArgGlyGluThrSerLeuGluLeuIleLeuSerThr 260
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                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        663 TCACCTAAAGGGACCCCAAATTCCAGAGGTGAAACAAGCCTGGAACTGATTCTATCAACC 722

Qy        261 ThrGlyTyrProPheSerSerProGluProGlySerAlaGlyHisSerArgIleSerThr 280
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        723 ACTGGATATCCCTTCTCCTCTCCTGAACCTGGCTCTGCAGGACACAGCAGAATAAGTACC 782

Qy        281 SerAlaProLeuSerSerSerAlaSerValLeuAspAsnLysIleSerGluThrSerIle 300
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        783 AGTGCGCCTTTGTCATCATCTGCTTCAGTTCTCGATAATAAAATATCAGAGACCAGCATA 842

Qy        301 PheSerGlyGlnSerLeuThrSerProLeuSerProGlyValProGluAlaArgAlaSer 320
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        843 TTCTCAGGCCAGAGTCTCACCTCCCCTCTGTCTCCTGGGGTGCCCGAGGCCAGAGCCAGC 902

Qy        321 ThrMetProAsnSerAlaIleProPheSerMetThrLeuSerAsnAlaGluThrSerAla 340
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        903 ACAATGCCCAACTCAGCTATCCCTTTTTCCATGACACTAAGCAATGCAGAAACAAGTGCC 962

Qy        341 GluArgValArgSerThrIleSerSerLeuGlyThrProSerIleSerThrLysGlnThr 360
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        963 GAAAGGGTCAGAAGCACAATTTCCTCTCTGGGGACTCCATCAATATCCACAAAGCAGACA 1022

Qy        361 AlaGluThrIleLeuThrPheHisAlaPheAlaGluThrMetAspIleProSerThrHis 380
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1023 GCAGAGACTATCCTTACCTTCCATGCCTTCGCTGAGACCATGGATATACCCAGCACCCAC 1082

Qy        381 IleAlaLysThrLeuAlaSerGluTrpLeuGlySerProGlyThrLeuGlyGlyThrSer 400
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1083 ATAGCCAAGACTTTGGCTTCAGAATGGTTGGGAAGTCCAGGTACCCTTGGTGGCACCAGC 1142

Qy        401 ThrSerAlaLeuThrThrThrSerProSerThrThrLeuValSerGluGluThrAsnThr 420
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1143 ACTTCAGCGCTGACAACCACATCTCCATCTACCACTTTAGTCTCAGAGGAGACCAACACC 1202

Qy        421 HisHisSerThrSerGlyLysGluThrGluGlyThrLeuAsnThrSerMetThrProLeu 440
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1203 CATCACTCCACGAGTGGAAAGGAGACAGAAGGAACTTTGAATACATCTATGACTCCACTT 1262

Qy        441 GluThrSerAlaProGlyGluGluSerGluMetThrAlaThrLeuValProThrLeuGly 460
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1263 GAGACCTCTGCTCCTGGAGAAGAGTCCGAAATGACTGCCACCTTGGTCCCCACTCTAGGT 1322

Qy        461 PheThrThrLeuAspSerLysIleArgSerProSerGlnValSerSerSerHisProThr 480
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1323 TTTACAACTCTTGACAGCAAGATCAGAAGTCCATCTCAGGTCTCTTCATCCCACCCAACA 1382

Qy        481 ArgGluLeuArgThrThrGlySerThrSerGlyArgGlnSerSerSerThrAlaAlaHis 500
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1383 AGAGAGCTCAGAACCACAGGCAGCACCTCTGGGAGGCAGAGTTCCAGCACAGCTGCCCAC 1442

Qy        501 GlySerSerAspIleLeuArgAlaThrThrSerSerThrSerLysAlaSerSerTrpThr 520
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1443 GGGAGCTCTGACATCCTGAGGGCAACCACTTCCAGCACCTCAAAAGCATCATCATGGACC 1502

Qy        521 SerGluSerThrAlaGlnGlnPheSerGluProGlnHisThrGlnTrpValGluThrSer 540
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1503 AGTGAAAGCACAGCTCAGCAATTTAGTGAACCCCAGCACACACAGTGGGTGGAGACAAGT 1562

Qy        541 ProSerMetLysThrGluArgProProAlaSerThrSerValAlaAlaProIleThrThr 560
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                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1563 CCTAGCATGAAAACAGAGAGACCCCCAGCATCAACCAGTGTGGCAGCCCCTATCACCACT 1622

Qy        561 SerValProSerValValSerGlyPheThrThrLeuLysThrSerSerThrLysGlyIle 580
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1623 TCTGTTCCCTCAGTGGTCTCTGGCTTCACCACCCTGAAGACCAGCTCCACAAAAGGGATT 1682

Qy        581 TrpLeuGluGluThrSerAlaAspThrLeuIleGlyGluSerThrAlaGlyProThrThr 600
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1683 TGGCTTGAAGAAACATCTGCAGACACACTCATCGGAGAATCCACAGCTGGCCCAACCACC 1742

Qy        601 HisGlnPheAlaValProThrGlyIleSerMetThrGlyGlySerSerThrArgGlySer 620
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1743 CATCAGTTTGCTGTTCCCACTGGGATTTCAATGACAGGAGGCAGCAGCACCAGGGGAAGC 1802

Qy        621 GlnGlyThrThrHisLeuLeuThrArgAlaThrAlaSerSerGluThrSerAlaAspLeu 640
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1803 CAGGGCACAACCCACCTACTCACCAGAGCCACAGCATCATCTGAGACATCCGCAGATTTG 1862

Qy        641 ThrLeuAlaThrAsnGlyValProValSerValSerProAlaValSerLysThrAlaAla 660
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1863 ACTCTGGCCACGAACGGTGTCCCAGTCTCCGTGTCTCCAGCAGTGAGCAAGACGGCTGCT 1922

Qy        661 GlySerSerProProGlyGlyThrLysProSerTyrThrMetValSerSerValIlePro 680
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1923 GGCTCAAGTCCTCCAGGAGGGACAAAGCCATCATATACAATGGTTTCTTCTGTCATCCCT 1982

Qy        681 GluThrSerSerLeuGlnSerSerAlaPheArgGluGlyThrSerLeuGlyLeuThrPro 700
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1983 GAGACATCATCTCTACAGTCCTCAGCTTTCAGGGAAGGAACCAGCCTGGGACTGACTCCA 2042

Qy        701 LeuAsnThrArgHisProPheSerSerProGluProAspSerAlaGlyHisThrLysIle 720
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2043 TTAAACACTAGACATCCCTTCTCTTCCCCTGAACCAGACTCTGCAGGACACACCAAGATA 2102

Qy        721 SerThrSerIleProLeuLeuSerSerAlaSerValLeuGluAspLysValSerAlaThr 740
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2103 AGCACCAGCATTCCTCTGTTGTCATCTGCTTCAGTTCTTGAGGATAAAGTGTCAGCGACC 2162

Qy        741 SerThrPheSerHisHisLysAlaThrSerSerIleThrThrGlyThrProGluIleSer 760
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2163 AGCACATTCTCACACCACAAAGCCACCTCATCTATTACCACAGGGACTCCTGAAATCTCA 2222

Qy        761 ThrLysThrLysProSerSerAlaValLeuSerSerMetThrLeuSerAsnAlaAlaThr 780
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2223 ACAAAGACAAAGCCCAGCTCAGCCGTTCTTTCCTCCATGACCCTAAGCAATGCAGCAACA 2282

Qy        781 SerProGluArgValArgAsnAlaThrSerProLeuThrHisProSerProSerGlyGlu 800
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2283 AGTCCTGAAAGAGTCAGAAATGCAACTTCCCCTCTGACTCATCCATCTCCATCAGGGGAA 2342

Qy        801 GluThrAlaGlySerValLeuThrLeuSerThrSerAlaGluThrThrAspSerProAsn 820
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2343 GAGACAGCAGGGAGTGTCCTCACTCTCAGCACCTCTGCTGAGACTACAGACTCACCTAAC 2402

Qy        821 IleHisProThrGlyThrLeuThrSerGluSerSerGluSerProSerThrLeuSerLeu 840
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2403 ATCCACCCAACTGGGACACTGACTTCAGAATCGTCAGAGAGTCCTAGCACTCTCAGCCTC 2462

Qy        841 ProSerValSerGlyValLysThrThrPheSerSerSerThrProSerThrHisLeuPhe 860
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                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2463 CCAAGTGTCTCTGGAGTCAAAACCACATTTTCTTCATCTACTCCTTCCACTCATCTATTT 2522

Qy        861 ThrSerGlyGluGluThrGluGluThrSerAsnProSerValSerGlnProGluThrSer 880
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2523 ACTAGTGGAGAAGAAACAGAGGAAACTTCGAATCCATCTGTGTCTCAACCTGAGACTTCT 2582

Qy        881 ValSerArgValArgThrThrLeuAlaSerThrSerValProThrProValProProThr 900
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2583 GTTTCCAGAGTAAGGACCACCTTGGCCAGCACCTCTGTCCCTACCCCAGTATTCCCCACC 2642

Qy        901 MetAspThrTrpProThrArgSerAlaGlnPheSerSerSerHisLeuValSerGluLeu 920
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2643 ATGGACACCTGGCCTACACGTTCAGCTCAGTTCTCTTCATCCCACCTAGTGAGTGAGCTC 2702

Qy        921 ArgAlaThrSerSerThrSerValThrAsnSerThrGlySerAlaLeuProLysIleSer 940
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2703 AGAGCTACGAGCAGTACCTCAGTTACAAACTCAACTGGTTCAGCTCTTCCTAAAATATCT 2762

Qy        941 HisLeuThrGlyThrAlaThrMetSerGlnThrAsnArgAspThrPheAsnAspSerAla 960
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2763 CACCTCACTGGGACGGCAACAATGTCACAGACCAATAGAGACACGTTTAATGACTCTGCT 2822

Qy        961 AlaProGlnSerThrThrTrpProGluThrSerProArgPheLysThrGlyLeuProSer 980
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2823 GCACCCCAAAGCACAACTTGGCCAGAGACTAGTCCCAGATTCAAGACAGGGTTACCTTCA 2882

Qy        981 AlaThrThrThrValSerThrSerAlaThrSerLeuSerAlaThrValMetValSerLys 1000
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2883 GCAACAACCACTGTTTCAACCTCTGCCACTTCTCTCTCTGCTACTGTAATGGTCTCTAAA 2942
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B. Alignment of amino acids 10,000-12,000 of SEQ ID NO: 5 to the sequences of Venter et al.

```
AFT04373
ID   AFT04373 standard; DNA; 25080 BP.
XX
AC   AFT04373;
XX
DT   20-SEP-2007  (first entry)
XX
DE   Human transcript sequence, SEQ ID 23771.
XX
KW   DNA detection; RNA detection; exon; ds.
XX
OS   Homo sapiens.
XX
PN   WO200268579-A2.
XX
PD   06-SEP-2002.
XX
PF   10-JAN-2002; 2002WO-US000284.
XX
PR   10-JAN-2001; 2001US-00756696.
XX
PA   (PEKE ) PE CORP NY.
XX
PI   Venter CJ,  Adams M,  Li PWD,  Myers EW;
XX
DR   WPI; 2002-682812/73.
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XX
PT   New isolated nucleic acid detection reagent for detecting the presence of
PT   specified human exons.
XX
PS   Claim 4; SEQ ID NO 23771; 40pp; English.
XX
CC   The present invention relates to a novel isolated nucleic acid detection
CC   reagent for detecting the presence of specified human exons. The exon
CC   sequences cover every identified human transcript and exon comprising
CC   every gene/coding region of the human genome. The present sequence is one
CC   such exon sequence. The nucleic acid detection agent is used for
CC   detecting the presence of at least 100000, at least 2000, at least 50000
CC   or at least 10000 human exons. The sequences that span exon-exon
CC   junctions eliminate false signals caused by genomic contamination. This
CC   is because a detection element comprising two neighboring exons as one
CC   contiguous sequence will not hybridize to genomic DNA comprising
CC   intervening intronic DNA. These detection elements will only hybridize to
CC   expressed mRNA transcripts in which the exons are connected and the
CC   intronic sequence has been removed, therefore forming one contiguous
CC   stretch of sequence corresponding to the sequence of the detection
CC   element that spans the exon-exon junction.
XX
SQ   Sequence 25080 BP; 6952 A; 7729 C; 4583 G; 5816 T; 0 U; 0 Other;

Alignment Scores:
Pred. No.:                3.2e-266        Length:         25080
Score:                    9274.50         Matches:        1870
Percent Similarity:       93.5%           Conservative:   0
Best Local Similarity:    93.5%           Mismatches:     8
Query Match:              92.8%           Indels:         123
DB:                       7               Gaps:           1

US-10-715-066A-5_COPY_10000_12000 (1-2001) x AFT04373 (1-25080)

Qy          1 ThrLeuMetSerArgSerProGluAsnProSerTrpLysSerSerProPheValGluLys 20
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      18568 ACTCTTATGAGTAGGAGTCCTGAAAATCCATCATGGAAGAGCTCTCCCTTTGTGGAAAAA 18627

Qy         21 ThrSerSerSerSerSerLeuLeuSerLeuProValThrThrSerProSerValSerSer 40
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      18628 ACTAGCTCTTCATCTTCTCTGTTGTCCTTACCTGTCACGACCTCACCTTCTGTTTCTTCC 18687

Qy         41 ThrLeuProGlnSerIleProSerSerSerPheSerValThrSerLeuLeuThrProGly 60
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      18688 ACATTACCGCAGAGTATCCCTTCCTCCTCTTTTTCTGTGACTTCACTCCTCACCCCAGGC 18747

Qy         61 MetValLysThrThrAspThrSerThrGluProGlyThrSerLeuSerProAsnLeuSer 80
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      18748 ATGGTGAAGACTACAGACACAAGCACAGAACCTGGAACCAGTTATCTCCAAATCTGAGT 18807

Qy         81 GlyThrSerValGluIleLeuAlaAlaSerGluValThrThrAspThrGluLysIleHis 100
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      18808 GGCACCTCAGTTGAAATACTGGCTGCCTCTGAAGTCACCACAGATACAGAGAAAATTCAT 18867

Qy        101 ProSerSerSerMetAlaValThrAsnValGlyThrThrSerSerGlyHisGluLeuTyr 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      18868 CCTTCTTCAAGCATGGCAGTGACCAATGTGGGAACCACCAGTTCTGGACATGAACTATAT 18927

Qy        121 SerSerValSerIleHisSerGluProSerLysAlaThrTyrProValGlyThrProSer 140
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
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Db      18928 TCCTCTGTTTCAATCCACTCGGAGCCATCCAAGGCTACATACCCAGTGGGTACTCCCTCT 18987

Qy        141 SerMetAlaGluThrSerIleSerThrSerMetProAlaAsnPheGluThrThrGlyPhe 160
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      18988 TCCATGGCTGAAACCTCTATTTCCACATCAATGCCTGCTAATTTTGAGACCACAGGATTT 19047

Qy        161 GluAlaGluProPheSerHisLeuThrSerGlyPheArgLysThrAsnMetSerLeuAsp 180
              ||||||||||||||||||||||||||||||||   ||||||||||||||||||||||||
Db      19048 GAGGCTGAGCCATTTTCTCATTTGACTTCTGGACTTAGGAAGACCAACATGTCCCTGGAC 19107

Qy        181 ThrSerSerValThrProThrAsnThrProSerSerProGlySerThrHisLeuLeuGln 200
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      19108 ACCAGCTCAGTCACACCAACAAATACACCTTCTTCTCCTGGGTCCACTCACCTTTTACAG 19167

Qy        201 SerSerLysThrAspPheThrSerSerAlaLysThrSerSerProAspTrpProProAla 220
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      19168 AGTTCCAAGACTGATTTCACCTCTTCTGCAAAAACATCATCCCCAGACTGGCCTCCAGCC 19227

Qy        221 SerGlnTyrThrGluIleProValAspIleIleThrProPheAsnAlaSerProSerIle 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      19228 TCACAGTATACTGAAATTCCAGTGGACATAATCACCCCCTTTAATGCTTCTCCATCTATT 19287

Qy        241 ThrGluSerThrGlyIleThrSerPheProGluSerArgPheThrMetSerValThrGlu 260
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      19288 ACGGAGTCCACTGGGATAACCTCCTTCCCAGAATCCAGGTTTACTATGTCTGTAACAGAA 19347

Qy        261 SerThrHisHisLeuSerThrAspLeuLeuProSerAlaGluThrIleSerThrGlyThr 280
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      19348 AGTACTCATCATCTGAGTACAGATTTGCTGCCTTCAGCTGAGACTATTTCCACTGGCACA 19407

Qy        281 ValMetProSerLeuSerGluAlaMetThrSerPheAlaThrThrGlyValProArgAla 300
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      19408 GTGATGCCTTCTCTATCAGAGGCCATGACTTCATTTGCCACCACTGGAGTTCCACGAGCC 19467

Qy        301 IleSerGlySerGlySerProPheSerArgThrGluSerGlyProGlyAspAlaThrLeu 320
              ||||||||||||||
Db      19468 ATCTCAGGTTCAGGA---------------------------------------------- 19482

Qy        321 SerThrIleAlaGluSerLeuProSerSerThrProValProPheSerSerSerThrPhe 340

Db      19482 ---------------------------------------------------------------- 19482

Qy        341 ThrThrThrAspSerSerThrIleProAlaLeuHisGluIleThrSerSerSerAlaThr 360

Db      19482 ---------------------------------------------------------------- 19482

Qy        361 ProTyrArgValAspThrSerLeuGlyThrGluSerSerThrThrGluGlyArgLeuVal 380

Db      19482 ---------------------------------------------------------------- 19482

Qy        381 MetValSerThrLeuAspThrSerSerGlnProGlyArgThrSerSerThrProIleLeu 400

Db      19482 ---------------------------------------------------------------- 19482

Qy        401 AspThrArgMetThrGluSerValGluLeuGlyThrValThrSerAlaTyrGlnValPro 420

Db      19482 ---------------------------------------------------------------- 19482

Qy        421 SerLeuSerThrArgLeuThrArgThrAspGlyIleMetGluHisIleThrLysIlePro 440
                              ||||||||||||||||||||||||||||||||||||||||
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Db      19483 -------------------------ACTGATGGCATTATGGAACACATCACAAAAATACCC 19518

Qy        441 AsnGluAlaAlaHisArgGlyThrIleArgProValLysGlyProGlnThrSerThrSer 460
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      19519 AATGAAGCAGCACACAGAGGTACCATAAGACCAGTCAAAGGCCCTCAGACATCCACTTCG 19578

Qy        461 ProAlaSerProLysGlyLeuHisThrGlyGlyThrLysArgMetGluThrThrThrThr 480
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      19579 CCTGCCAGTCCTAAAGGACTACACACAGGAGGGACAAAAAGAATGGAGACCACCACCACA 19638

Qy        481 AlaLeuLysThrThrThrThrAlaLeuLysThrThrSerArgAlaThrLeuThrThrSer 500
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      19639 GCTCTGAAGACCACCACCACAGCTCTGAAGACCACTTCCAGAGCCACCTTGACCACCAGT 19698

Qy        501 ValTyrThrProThrLeuGlyThrLeuThrProLeuAsnAlaSerArgGlnMetAlaSer 520
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      19699 GTCTATACTCCCACTTTGGGAACACTGACTCCCCTCAATGCATCAATGCAAATGGCCAGC 19758

Qy        521 ThrIleLeuThrGluMetMetIleThrThrProTyrValPheProAspValProGluThr 540
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      19759 ACAATCCCCACAGAAATGATGATCACAACCCCATATGTTTTCCCTGATGTTCCAGAAACG 19818

Qy        541 ThrSerSerLeuAlaThrSerLeuGlyAlaGluThrSerThrAlaLeuProArgThrThr 560
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      19819 ACATCCTCATTGGCTACCAGCCTGGGAGCAGAAACCAGCACAGCTCTTCCCAGGACAACC 19878

Qy        561 ProSerValLeuAsnArgGluSerGluThrThrAlaSerLeuValSerArgSerGlyAla 580
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      19879 CCATCTGTTTTCAATAGAGAATCAGAGACCACAGCCTCACTGGTCTCTCGTTCTGGGGCA 19938

Qy        581 GluArgSerProValIleGlnThrLeuAspValSerSerSerGluProAspThrThrAla 600
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      19939 GAGAGAAGTCCGGTTATTCAAACTCTAGATGTTTCTTCTAGTGAGCCAGATACAACAGCT 19998

Qy        601 SerTrpValIleHisProAlaGluThrIleProThrValSerLysThrThrProAsnPhe 620
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      19999 TCATGGGTTATCCATCCTGCAGAGACCATCCCAACTGTTTCCAAGACAACCCCCAATTTT 20058

Qy        621 PheHisSerGluLeuAspThrValSerSerThrAlaThrSerHisGlyAlaAspValSer 640
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      20059 TTCCACAGTGAATTAGACACTGTATCTTCCACAGCCACCAGTCATGGGGCAGACGTCAGC 20118

Qy        641 SerAlaIleProThrAsnIleSerProSerGluLeuAspAlaLeuThrProLeuValThr 660
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      20119 TCAGCCATTCCAACAAATATCTCACCTAGTGAACTAGATGCACTGACCCCACTGGTCACT 20178

Qy        661 IleSerGlyThrAspThrSerThrThrProThrLeuThrLysSerProHisGluThr 680
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      20179 ATTTCGGGGACAGATACTAGTACAACATTCCCAACACTGACTAAGTCCCCACATGAAACA 20238

Qy        681 GluThrArgThrThrTrpLeuThrHisProAlaGluThrSerSerThrIleProArgThr 700
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      20239 GAGACAAGAACCACATGGCTCACTCATCCTGCAGAGACCAGCTCAACTATTCCCAGAACA 20298

Qy        701 IleProAsnPheSerHisHisGluSerAspAlaThrProSerIleAlaThrSerProGly 720
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      20299 ATCCCCAATTTTTCTCATCATGAATCAGATGCCACACCTTCAATAGCCACCAGTCCTGGG 20358

Qy        721 AlaGluThrSerSerAlaIleProIleMetThrValSerProGlyAlaGluAspLeuVal 740
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
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Db      20359 GCAGAAACCAGTTCAGCTATTCCAATTATGACTGTCTCACCTGGTGCAGAAGATCTGGTG 20418

Qy        741 ThrSerGlnValThrSerSerGlyThrAspArgAsnMetThrIleProThrLeuThrLeu 760
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      20419 ACCTCACAGGTCACTAGTTCTGGCACAGACAGAAATATGACTATTCCAACTTTGACTCTT 20478

Qy        761 SerProGlyGluProLysThrIleAlaSerLeuValThrHisProGluAlaGlnThrSer 780
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      20479 TCTCCTGGTGAACCAAAGACCATAGCCTCATTAGTCACCCATCCTGAAGCACAGACAAGT 20538

Qy        781 SerAlaIleProThrSerThrIleSerProAlaValSerArgLeuValThrSerMetVal 800
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      20539 TCGGCCATTCCAACTTCAACTATCTCGCCTGCTGTATCACGGTTGGTGACCTCAATGGTC 20598

Qy        801 ThrSerLeuAlaAlaLysThrSerThrThrAsnArgAlaLeuThrAsnSerProGlyGlu 820
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      20599 ACCAGTTTGGCGGCAAAGACAAGTACAACTAATCGAGCTCTGACAAACTCCCCTGGTGAA 20658

Qy        821 ProAlaThrThrValSerLeuValThrHisProAlaGlnThrSerProThrValProTrp 840
              ||||||||||||||||||||||||||||||||    ||||||||||||||||||||||||||||
Db      20659 CCAGCTACAACAGTTTCATTGGTCACGCATTCTGCACAGACCAGCCCAACAGTTCCCTGG 20718

Qy        841 ThrThrSerIlePhePheHisSerLysSerAspThrThrProSerMetThrThrSerHis 860
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      20719 ACAACTTCCATTTTTTTCCATAGTAAATCAGACACCACACCTTCAATGACCACCAGTCAT 20778

Qy        861 GlyAlaGluSerSerSerAlaValProThrProThrValSerThrGluValProGlyVal 880
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      20779 GGGGCAGAATCCAGTTCAGCTGTTCCAACTCCAACTGTTTCAACTGAGGTACCAGGAGTA 20838

Qy        881 ValThrProLeuValThrSerSerArgAlaValIleSerThrThrIleProIleLeuThr 900
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      20839 GTGACCCCTTTGGTCACCAGTTCTAGGGCAGTGATCAGTACAACTATTCCAATTCTGACT 20898

Qy        901 LeuSerProGlyGluProGluThrThrProSerMetAlaThrSerHisGlyGluGluAla 920
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      20899 CTTTCTCCTGGTGAACCAGAGACCACACCTTCAATGGCCACCAGTCATGGGGAAGAAGCC 20958

Qy        921 SerSerAlaIleProThrProThrValSerProGlyValProGlyValValThrSerLeu 940
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      20959 AGTTCTGCTATTCCAACTCCAACTGTTTCACCTGGGGTACCAGGAGTGGTGACCTCTCTG 21018

Qy        941 ValThrSerSerArgAlaValThrSerThrThrIleProIleLeuThrPheSerLeuGly 960
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      21019 GTCACTAGTTCTAGGGCAGTGACTAGTACAACTATTCCAATTCTGACTTTTTCTCTTGGT 21078

Qy        961 GluProGluThrThrProSerMetAlaThrSerHisGlyThrGluAlaGlySerAlaVal 980
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      21079 GAACCAGAGACCACACCTTCAATGGCCACCAGTCATGGGACAGAAGCTGGCTCAGCTGTT 21138

Qy        981 ProThrValLeuProGluValProGlyMetValThrSerLeuValAlaSerSerArgAla 1000
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      21139 CCAACTGTTTTACCTGAGGTACCAGGAATGGTGACCTCTCTGGTTGCTAGTTCTAGGGCA 21198

Qy       1001 ValThrSerThrThrLeuProThrLeuThrLeuSerProGlyGluProGluThrThrPro 1020
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      21199 GTAACCAGTACAACTCTTCCAACTCTGACTCTTTCTCCTGGTGAACCAGAGACCACACCT 21258

Qy       1021 SerMetAlaThrSerHisGlyAlaGluAlaSerSerThrValProThrValSerProGlu 1040
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
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Db      21259 TCAATGGCCACCAGTCATGGGGCAGAAGCCAGCTCAACTGTTCCAACTGTTTCACCTGAG 21318

Qy       1041 ValProGlyValValThrSerLeuValThrSerSerSerGlyValAsnSerThrSerIle 1060
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      21319 GTACCAGGAGTGGTGACCTCTCTGGTCACTAGTTCTAGTGGAGTAAACAGTACAAGTATT 21378

Qy       1061 ProThrLeuIleLeuSerProGlyGluLeuGluThrThrProSerMetAlaThrSerHis 1080
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      21379 CCAACTCTGATTCTTTCTCCTGGTGAACTAGAAACCACACCTTCAATGGCCACCAGTCAT 21438

Qy       1081 GlyAlaGluAlaSerSerAlaValProThrProThrValSerProGlyValSerGlyVal 1100
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      21439 GGGGCAGAAGCCAGCTCAGCTGTTCCAACTCCAACTGTTCACCTGGGGTATCAGGAGTG 21498

Qy       1101 ValThrProLeuValThrSerSerArgAlaValThrSerThrThrIleProIleLeuThr 1120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      21499 GTGACCCCTCTGGTCACTAGTTCCAGGGCAGTGACCAGTACAACTATTCCAATTCTAACT 21558

Qy       1121 LeuSerSerSerGluProGluThrThrProSerMetAlaThrSerHisGlyValGluAla 1140
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      21559 CTTTCTTCTAGTGAGCCAGAGACCACACCTTCAATGGCCACCAGTCATGGGGTAGAAGCC 21618

Qy       1141 SerSerAlaValLeuThrValSerProGluValProGlyMetValThrSerLeuValThr 1160
              ||||||||||||||||||||||||||||||||||||||||||||    |||||||||
Db      21619 AGCTCAGCTGTTCTAACTGTTTCACCTGAGGTACCAGGAATGGTGACCTTTCTGGTCACT 21678

Qy       1161 SerSerArgAlaValThrSerThrThrIleProThrLeuThrIleSerSerAspGluPro 1180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      21679 AGTTCTAGAGCAGTAACCAGTACAACTATTCCAACTCTGACTATTTCTTCTGATGAACCA 21738

Qy       1181 GluThrThrThrSerLeuValThrHisSerGluAlaLysMetIleSerAlaIleProThr 1200
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      21739 GAGACCACAACTTCATTGGTCACCCATTCTGAGGCAAAGATGATTTCAGCCATTCCAACT 21798

Qy       1201 LeuAlaValSerProThrValGlnGlyLeuValThrSerLeuValThrSerSerGlySer 1220
              |||   ||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      21799 TTAGGTGTCTCCCCTACTGTACAAGGGCTGGTGACTTCACTGGTCACTAGTTCTGGGTCA 21858

Qy       1221 GluThrSerAlaPheSerAsnLeuThrValAlaSerSerGlnProGluThrIleAspSer 1240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      21859 GAGACCAGTGCGTTTTCAAATCTAACTGTTGCCTCAAGTCAACCAGAGACCATAGACTCA 21918

Qy       1241 TrpValAlaHisProGlyThrGluAlaSerSerValValProThrLeuThrValSerThr 1260
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      21919 TGGGTCGCTCATCCTGGGACAGAAGCAAGTTCTGTTGTTCCAACTTTGACTGTCTCCACT 21978

Qy       1261 GlyGluProPheThrAsnIleSerLeuValThrHisProAlaGluSerSerSerThrLeu 1280
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      21979 GGTGAGCCGTTTACAAATATCTCATTGGTCACCCATCCTGCAGAGAGTAGCTCAACTCTT 22038

Qy       1281 ProArgThrThrSerArgPheSerHisSerGluLeuAspThrMetProSerThrValThr 1300
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      22039 CCCAGGACAACCTCAAGGTTTTCCCACAGTGAATTAGACACTATGCCTTCTACAGTCACC 22098

Qy       1301 SerProGluAlaGluSerSerSerAlaIleSerThrThrIleSerProGlyIleProGly 1320
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      22099 AGTCCTGAGGCAGAATCCAGCTCAGCCATTTCAACAACTATTTCACCTGGTATACCAGGT 22158

Qy       1321 ValLeuThrSerLeuValThrSerSerGlyArgAspIleSerAlaThrProProThrVal 1340
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
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Db      22159 GTGCTGACATCACTGGTCACTAGCTCTGGGAGAGACATCAGTGCAACTTTTCCAACAGTG 22218

Qy       1341 ProGluSerProHisGluSerGluAlaThrAlaSerTrpValThrHisProAlaValThr 1360
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      22219 CCTGAGTCCCCACATGAATCAGAGGCAACAGCCTCATGGGTTACTCATCCTGCAGTCACC 22278

Qy       1361 SerThrThrValProArgThrThrProAsnTyrSerHisSerGluProAspThrThrPro 1380
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      22279 AGCACAACAGTTCCCAGGACAACCCCTAATTATTCTCATAGTGAACCAGACACCACACCA 22338

Qy       1381 SerIleAlaThrSerProGlyAlaGluAlaThrSerAspPheProThrIleThrValSer 1400
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      22339 TCAATAGCCACCAGTCCTGGGGCAGAAGCCACTTCAGATTTTCCAACAATAACTGTCTCA 22398

Qy       1401 ProAspValProAspMetValThrSerGlnValThrSerSerGlyThrAspThrSerIle 1420
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      22399 CCTGATGTACCAGATATGGTAACCTCACAGGTCACTAGTTCTGGGACAGACACCAGTATA 22458

Qy       1421 ThrIleProThrLeuThrLeuSerSerGlyGluProGluThrThrThrSerPheIleThr 1440
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      22459 ACTATTCCAACTCTGACTCTTTCTTCTGGTGAGCCAGAGACCACAACCTCATTTATCACC 22518

Qy       1441 TyrSerGluThrHisThrSerSerAlaIleProThrLeuProValSerProGlyAlaSer 1460
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      22519 TATTCTGAGACACATACAAGTTCAGCCATTCCAACTCTCCCTGTCTCCCCTGATGCATCA 22578

Qy       1461 LysMetLeuThrSerLeuValIleSerSerGlyThrAspSerThrThrThrProProThr 1480
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      22579 AAGATGCTGACCTCACTGGTCATCAGTTCTGGGACAGACAGCACTACAACTTTCCCAACA 22638

Qy       1481 LeuThrGluThrProTyrGluProGluThrThrAlaIleGlnLeuIleHisProAlaGlu 1500
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      22639 CTGACGGAGACCCCATATGAACCAGAGACAACAGCCATACAGCTCATTCATCCTGCAGAG 22698

Qy       1501 ThrAsnThrMetValProArgThrThrProLysPheSerHisSerLysSerAspThrThr 1520
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      22699 ACCAACACAATGGTTCCCAGGACAACTCCCAAGTTTTCCCATAGTAAGTCAGACACCACA 22758

Qy       1521 LeuProValAlaIleThrSerProGlyProGluAlaSerSerAlaValSerThrThrThr 1540
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      22759 CTCCCAGTAGCCATCACCAGTCCTGGGCCAGAAGCCAGTTCAGCTGTTTCAACGACAACT 22818

Qy       1541 IleSerProAspMetSerAspLeuValThrSerLeuValProSerSerGlyThrAspThr 1560
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      22819 ATCTCACCTGATATGTCAGATCTGGTGACCTCACTGGTCCCTAGTTCTGGGACAGACACC 22878

Qy       1561 SerThrThrProProThrLeuSerGluThrProTyrGluProGluThrThrAlaThrTrp 1580
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      22879 AGTACAACCTTCCCAACATTGAGTGAGACCCCATATGAACCAGAGACTACAGCCACGTGG 22938

Qy       1581 LeuThrHisProAlaGluThrSerThrThrValSerGlyThrIleProAsnPheSerHis 1600
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      22939 CTCACTCATCCTGCAGAAACCAGCACAACGGTTTCTGGGACAATTCCCAACTTTTCCCAT 22998

Qy       1601 ArgGlySerAspThrAlaProSerMetValThrSerProGlyValAspThrArgSerGly 1620
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      22999 AGGGGATCAGACACTGCACCCTCAATGGTCACCAGTCCTGGAGTAGACACGAGGTCAGGT 23058

Qy       1621 ValProThrThrThrIleProProSerIleProGlyValValThrSerGlnValThrSer 1640
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
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Db      23059 GTTCCAACTACAACCATCCCACCCAGTATACCAGGGGTAGTGACCTCACAGGTCACTAGT 23118

Qy       1641 SerAlaThrAspThrSerThrAlaIleProThrLeuThrProSerProGlyGluProGlu 1660
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      23119 TCTGCAACAGACACTAGTACAGCTATTCCAACTTTGACTCCTTCTCCTGGTGAACCAGAG 23178

Qy       1661 ThrThrAlaSerSerAlaThrHisProGlyThrGlnThrGlyPheThrValProIleArg 1680
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      23179 ACCACAGCCTCATCAGCTACCCATCCTGGGACACAGACTGGCTTCACTGTTCCAATTCGG 23238

Qy       1681 ThrValProSerSerGluProAspThrMetAlaSerTrpValThrHisProProGlnThr 1700
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      23239 ACTGTTCCCTCTAGTGAGCCAGATACAATGGCTTCCTGGGTCACTCATCCTCCACAGACC 23298

Qy       1701 SerThrProValSerArgThrThrSerSerPheSerHisSerSerProAspAlaThrPro 1720
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      23299 AGCACACCTGTTTCCAGAACCAACCTCCAGTTTTTCCCATAGTAGTCCAGATGCCACACCT 23358

Qy       1721 ValMetAlaThrSerProArgThrGluAlaSerSerAlaValLeuThrThrIleSerPro 1740
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      23359 GTAATGGCCACCAGTCCTAGGACAGAAGCCAGTTCAGCTGTACTGACAACAATCTCACCT 23418

Qy       1741 GlyAlaProGluMetValThrSerGlnIleThrSerSerGlyAlaAlaThrSerThrThr 1760
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      23419 GGTGCACCAGAGATGGTGACTTCACAGATCACTAGTTCTGGGGCAGCAACCAGTACAACT 23478

Qy       1761 ValProThrLeuThrHisSerProGlyMetProGluThrThrAlaLeuLeuSerThrHis 1780
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      23479 GTTCCAACTTTGACTCATTCTCCTGGTATGCCAGAGACCACAGCCTTATTGAGCACCCAT 23538

Qy       1781 ProArgThrGluThrSerLysThrProProAlaSerThrValProProGlnValSerGlu 1800
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      23539 CCCAGAACAGAGACAAGTAAAACATTTCCTGCTTCAACTGTGTTTCCTCAAGTATCAGAG 23598

Qy       1801 ThrThrAlaSerLeuThrIleArgProGlyAlaGluThrSerThrAlaLeuProThrGln 1820
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      23599 ACCACAGCCTCACTCACCATTAGACCTGGTGCAGAGACTAGCACAGCTCTCCCAACTCAG 23658

Qy       1821 ThrThrSerSerLeuPheThrLeuLeuValThrGlyThrSerArgValAspLeuSerPro 1840
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      23659 ACAACATCCTCTCTCTTCACCCTACTTGTAACTGGAACCAGCAGAGTTGATCTAAGTCCA 23718

Qy       1841 ThrAlaSerProGlyValSerAlaLysThrAlaProLeuSerThrHisProGlyThrGlu 1860
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      23719 ACTGCTTCACCTGGTGTTTCTGCAAAAACAGCCCCACTTTCCACCCATCCAGGGACAGAA 23778

Qy       1861 ThrSerThrMetIleProThrSerThrLeuSerLeuGlyLeuLeuGluThrThrGlyLeu 1880
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      23779 ACCAGCACAATGATTCCAACTTCAACTCTTTCCCTTGGTTTACTAGAGACTACAGGCTTA 23838

Qy       1881 LeuAlaThrSerSerSerAlaGluThrSerThrSerThrLeuThrLeuThrValSerPro 1900
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      23839 CTGGCCACCAGCTCTTCAGCAGAGACCAGCACGAGTACTCTAACTCTGACTGTTTCCCCT 23898

Qy       1901 AlaValSerGlyLeuSerSerAlaSerIleThrThrAspLysProGlnThrValThrSer 1920
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      23899 GCTGTCTCTGGGCTTTCCAGTGCCTCTATAACAACTGATAAGCCCCAAACTGTGACCTCC 23958

Qy       1921 TrpAsnThrGluThrSerProSerValThrSerValGlyProProGluPheSerArgThr 1940
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
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Db      23959 TGGAACACAGAAACCTCACCATCTGTAACTTCAGTTGGACCCCCAGAATTTTCCAGGACT 24018

Qy       1941 ValThrGlyThrThrMetThrLeuIleProSerGluMetProThrProProLysThrSer 1960
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      24019 GTCACAGGCACCACTATGACCTTGATACCATCAGAGATGCCAACACCACCTAAAACCAGT 24078

Qy       1961 HisGlyGluGlyValSerProThrThrIleLeuArgThrThrMetValGluAlaThrAsn 1980
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      24079 CATGGAGAAGGAGTGAGTCCAACCACTATCTTGAGAACTACAATGGTTGAAGCCACTAAT 24138

Qy       1981 LeuAlaThrThrGlySerSerProThrValAlaLysThrThrThrPheAsnThrLeu 2000
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      24139 TTAGCTACCACAGGTTCCAGTCCCACTGTGGCCAAGACAACAACCACCTTCAATACACTG 24198

Qy       2001 Ala 2001
              |||
Db      24199 GCT 24201
```

C. Alignment of amino acids 19,152-21,152 of SEQ ID NO: 5 to the sequences of Venter et al.

```
AFS86217
ID   AFS86217 standard; DNA; 568 BP.
XX
AC   AFS86217;
XX
DT   20-SEP-2007  (first entry)
XX
DE   Human transcript sequence, SEQ ID 5616.
XX
KW   DNA detection; RNA detection; exon; ds.
XX
OS   Homo sapiens.
XX
PN   WO200268579-A2.
XX
PD   06-SEP-2002.
XX
PF   10-JAN-2002; 2002WO-US000284.
XX
PR   10-JAN-2001; 2001US-00756696.
XX
PA   (PEKE ) PE CORP NY.
XX
PI   Venter CJ,  Adams M,  Li PWD,  Myers EW;
XX
DR   WPI; 2002-682812/73.
XX
PT   New isolated nucleic acid detection reagent for detecting the presence of
PT   specified human exons.
XX
PS   Claim 4; SEQ ID NO 5616; 40pp; English.
XX
CC   The present invention relates to a novel isolated nucleic acid detection
CC   reagent for detecting the presence of specified human exons. The exon
CC   sequences cover every identified human transcript and exon comprising
CC   every gene/coding region of the human genome. The present sequence is one
CC   such exon sequence. The nucleic acid detection agent is used for
CC   detecting the presence of at least 100000, at least 2000, at least 50000
CC   or at least 10000 human exons. The sequences that span exon-exon
CC   junctions eliminate false signals caused by genomic contamination. This
```

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CC   is because a detection element comprising two neighboring exons as one
CC   contiguous sequence will not hybridize to genomic DNA comprising
CC   intervening intronic DNA. These detection elements will only hybridize to
CC   expressed mRNA transcripts in which the exons are connected and the
CC   intronic sequence has been removed, therefore forming one contiguous
CC   stretch of sequence corresponding to the sequence of the detection
CC   element that spans the exon-exon junction.
XX
SQ   Sequence 568 BP; 149 A; 168 C; 131 G; 120 T; 0 U; 0 Other;

Alignment Scores:
Pred. No.:              2.06e-59        Length:         568
Score:                  996.00          Matches:        188
Percent Similarity:     100.0%          Conservative:   0
Best Local Similarity:  100.0%          Mismatches:     0
Query Match:            6.7%            Indels:         0
DB:                     7               Gaps:           0

US-10-715-066A-5_COPY_19152_22152 (1-3001) x AFS86217 (1-568)

Qy       2814 ThrGlnHisPheTyrLeuAsnPheThrIleThrAsnLeuProTyrSerGlnAspLysAla 2833
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          2 ACCCAGCACTTCTACCTGAATTTCACCATCACCAACCTACCATATTCCCAGGACAAAGCC 61

Qy       2834 GlnProGlyThrThrAsnTyrGlnArgAsnLysArgAsnIleGluAspAlaLeuAsnGln 2853
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         62 CAGCCAGGCACCACCAATTACCAGAGGAACAAAAGGAATATTGAGGATGCGCTCAACCAA 121

Qy       2854 LeuPheArgAsnSerSerIleLysSerTyrPheSerAspCysGlnValSerThrPheArg 2873
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        122 CTCTTCCGAAACAGCAGCATCAAGAGTTATTTTTCTGACTGTCAAGTTTCAACATTCAGG 181

Qy       2874 SerValProAsnArgHisHisThrGlyValAspSerLeuCysAsnPheSerProLeuAla 2893
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        182 TCTGTCCCCAACAGGCACCACACCGGGGTGGACTCCCTGTGTAACTTCTCGCCACTGGCT 241

Qy       2894 ArgArgValAspArgValAlaIleTyrGluGluPheLeuArgMetThrArgAsnGlyThr 2913
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        242 CGGAGAGTAGACAGAGTTGCCATCTATGAGGAATTTCTGCGGATGACCCGGAATGGTACC 301

Qy       2914 GlnLeuGlnAsnPheThrLeuAspArgSerSerValLeuValAspGlyTyrSerProAsn 2933
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        302 CAGCTGCAGAACTTCACCCTGGACAGGAGCAGTGTCCTTGTGGATGGGTATTCTCCCCAAC 361

Qy       2934 ArgAsnGluProLeuThrGlyAsnSerAspLeuProPheTrpAlaValIleLeuIleGly 2953
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        362 AGAAATGAGCCCTTAACTGGGAATTCTGACCTTCCCTTCTGGGCTGTCATCCTCATCGGC 421

Qy       2954 LeuAlaGlyLeuLeuGlyLeuIleThrCysLeuIleCysGlyValLeuValThrThrArg 2973
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        422 TTGGCAGGACTCCTGGGACTCATCACATGCCTGATCTGCGGTGTCCTGGTGACCACCCGC 481

Qy       2974 ArgArgLysLysGluGlyGluTyrAsnValGlnGlnGlnCysProGlyTyrTyrGlnSer 2993
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        482 CGGCGGAAGAAGGAAGGAGAATACAACGTCCAGCAACAGTGCCCAGGCTACTACCAGTCA 541

Qy       2994 HisLeuAspLeuGluAspLeuGln 3001
              |||||||||||||||||||||||||
Db        542 CACCTAGACCTGGAGGATCTGCAA 565
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Appendix 3
Alignment of amino acids 19,152-21,152 of SEQ ID NO: 5 to the sequences of Algate et al.

```
AAH83663/c
ID   AAH83663 standard; cDNA; 643 BP.
XX
AC   AAH83663;
XX
DT   25-SEP-2001  (first entry)
XX
DE   Human ovarian tumour associated polynucleotide sequence SEQ ID NO:1287.
XX
KW   Human; ovarian tumour; ovarian cancer; diagnosis; gene therapy;
KW   immunogenic; vaccine; ss.
XX
OS   Homo sapiens.
XX
PN   WO200151513-A2.
XX
PD   19-JUL-2001.
XX
PF   16-JAN-2001; 2001WO-US001575.
XX
PR   14-JAN-2000; 2000US-0176722P.
XX
PA   (CORI-) CORIXA CORP.
XX
PI   Algate PA;
XX
DR   WPI; 2001-425866/45.
XX
PT   Novel ovarian tumor proteins, and nucleic acids encoding them, used to
PT   treat and diagnose cancers, particularly ovarian cancer.
XX
PS   Claim 5; Page 298; 338pp; English.
XX
CC   AAH82377 to AAH83878 represent human ovarian tumour-associated
CC   polynucleotide sequences which encode ovarian tumour proteins. The
CC   ovarian tumour protein and polynucleotide sequences have cytostatic
CC   activity, and can be used in gene therapy and vaccine production. The
CC   ovarian tumour proteins and polynucleotides can be used to inhibit the
CC   development of cancer, particularly ovarian cancer. They can also be used
CC   to diagnose the onset and progression of cancer
XX
SQ   Sequence 643 BP; 144 A; 151 C; 180 G; 163 T; 0 U; 5 Other;

Alignment Scores:
Pred. No.:              1.35e-48       Length:        643
Score:                  840.50         Matches:       167
Percent Similarity:     96.5%          Conservative:  0
Best Local Similarity:  96.5%          Mismatches:    1
Query Match:            5.7%           Indels:        6
DB:                     4              Gaps:          1

US-10-715-066A-5_COPY_19152_22152 (1-3001) x AAH83663 (1-643)

Qy       2747 ThrAsnLeuThrMetAspSerValLeuValThrValLysAlaLeuPheSerSerAsnLeu 2766
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        518 ACCAACTTGACGATGGACTCCGTGTTGGTCACTGTCAAGGCATTGTTCTCCTCCAATTTG 459
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Qy       2767 AspProSerLeuValGluGlnValPheLeuAspLysThrLeuAsnAlaSerPheHisTrp 2786
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        458 GACCCCAGCCTGGTGGAGCAAGTCTTTCTAGATAAGACCCTGAATGCCTCATTCCATTGG 399

Qy       2787 LeuGlySerThrTyrGlnLeuValAspIleHisValThrGluMetGluSerSerValTyr 2806
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        398 CTGGGCTCCACCTACCAGTTGGTGGACATCCATGTGACAGAAATGGAGTCATCAGTTTAT 339

Qy       2807 GlnProThrSerSerSerSerThrGlnHisPheTyrLeuAsnPheThrIleThrAsnLeu 2826
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        338 CAACCAACAAGCAGCTCCAGCACCCAGCACTTCTACCTGAATTTCACCATCACCAACCTA 279

Qy       2827 ProTyrSerGlnAspLysAlaGlnProGlyThrThrAsnTyrGlnArgAsnLysArgAsn 2846
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        278 CCATATTCCCAGGACAAAGCCCAGCCAGGCACCACCAATTACCAGAGGAACAAAAGGAAT 219

Qy       2847 IleGluAspAla----------------LeuAsnGlnLeuPheArgAsnSerSerIleLys 2861
             |||||||||                    ||||||||||||||||||||||||||||||||||
Db        218 ATTGAGGATGC-GGTGAGAAGGGGGTGCTCAACCAACTCTTCCGAAACAGCAGCATCAAG 160

Qy       2862 SerTyrPheSerAspCysGlnValSerThrPheArgSerValProAsnArgHisHisThr 2881
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        159 AGTTATTTTTCTGACTGTCAAGTTTCAACATTCAGGTCTGTCCCCAACAGGCACCACACC 100

Qy       2882 GlyValAspSerLeuCysAsnPheSerProLeuAlaArgArgValAspArgValAlaIle 2901
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         99 GGGGTGGACTCCCTGTGTAACTTCTCGCCACTGGCTCGGAGAGTAGACAGAGTTGCCATC 40

Qy       2902 TyrGluGluPheLeuArgMetThrArgAsnGlyThrGln 2914
             ||||||||||||||||||||||||||||||||||||||
Db         39 TATGAGGAATTTCTGCGGATGACCCGGAATGGTACCCAG 1
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